REMARKS

Claims 17, 20, 21 and 40 presently appear in this case. No claims have been allowed. The official action of July 6, 2007, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to an RNA molecule that targets mRNA corresponding to the DNA of SEQ ID NO:2. The targeting preferably prevents processing, splicing, transport or translation of the mRNA or results in mRNA degradation. The RNA may be an antisense RNA or a ribozyme.

The examiner states that the present claims are not supported by provisional application no. 60/056,453 as there is no disclosure of SEQ ID NO:2 or 10 therein. The examiner states that prior filed applications 09/138,112 and 09/604,978 disclose SEQ ID NO:2, but neither they nor the present application support the present claims because of the new matter rejection. Therefore, the examiner considers that the effective filing date of the present claims, in which the limitation reads on SEQ ID NO:2, is August 21, 1998, but the limitation for the present claims referring to a nucleic acid encoding SEQ ID NO:10 is considered to be the filing date of the amendment filed on September 8, 2006.

The claims have now been amended to refer to SEQ ID NO:2 rather than SEQ ID NO:10. Thus, it is apparently the

examiner's position that the present claims are entitled to an effective filing date of August 21, 1998. As to the examiner's consideration that the effective filing date of the present claims is September 8, 2006, that will be discussed hereinbelow with respect to the prior art rejection.

The examiner states that the declaration is defective and that a new declaration is required because the amendment filed on March 17, 2004, introduced claims that contained new matter. This requirement is respectfully traversed.

There is nothing in MPEP 602.01 or 602.02 that says that an amendment attempting to introduce alleged new matter makes a declaration defective. Indeed, 37 CFR 1.67(b) explicitly states:

> No new matter may be introduced into a nonprovisional application after its filing date even if a supplemental oath or declaration is filed.

Thus, the filing of a supplement oath or declaration will not affect alleged new matter rejection one way or another. What then is the purpose of requiring that a new declaration be filed? Reconsideration and withdrawal of this requirement is respectfully urged. In any event, the alleged new matter has now been removed from the claims, thus obviating this requirement.

Claims 17, 20, 21 and 40 have been rejected under 35 U.S.C. 101, because the claimed invention is not supported by a substantial or well established utility. The examiner states that the specification provides no nexus between the the claimed nucleic acid molecule with regulating angiogenesis or apoptosis. The examiner states that the specification does not teach what to look for as a result of an increase or a decrease in expression of SEQ ID NO:10. The examiner states that the specification provides no evidence that the claimed DNA sequences are associated with any specific disease and it would require further experimentation to determine whether the sequences are involved in hypoxic conditions or other diseases. Thus, the examiner states that the asserted utilities do not provide a benefit to the public in currently available form. This rejection is respectfully traversed.

Many utilities are disclosed for the antisense molecules in accordance with the present invention. However, only one such utility is necessary in order to satisfy 35 U.S.C. 101. See MPEP 2107 II(B)(1)(ii) where it states:

> An applicant need only provide one credible assertion of specific and substantial utility for each claimed invention to satisfy the utility requirement.

Note further in MPEP 2107 where the MPEP states:

> Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted

> utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement.

The present specification has several statements of utility for the antibody technology. Note, for example, paragraph [0012] where it states that the administration of an antisense oligonucleotide directed against SEQ ID NO:2 provides "a method of regulating response to ischemic or hypoxic conditions in a patient in need of such treatment." See also paragraph [0054] and [0055] on page 22 which also speak of the use of an antagonist for a protein of SEQ ID NO:10 for the treatment of a subject in need of treatment for hypoxia or ischemia-related disease (such as stroke). See also paragraph [0053] where it states that an antisense oligonucleotide can be used to regulate apoptosis in a patient in need of such treatment. These assertions of utility are specific and substantial. They certainly satisfy the requirements of 35 U.S.C. 101. The examiner has not submitted sufficient evidence to establish a *prima facie* case that the presumptively accurate statements in the present specification are incredible.

Furthermore, much work has been done confirming a utility for down-regulation of RTP801 expression. Today, the human protein is known as RTP801. See, for example, GenBank

entry Q9NX09, defining the human RTP801 protein and indicating that the name is synonymous with DEPP1 and DDIT4. Note the sequence provided (copy submitted herewith). Also attached herewith are the following abstracts or publications:

Gery et al., "RTP801 is a Novel Retinoic Acid-Responsive Gene Associated with Myeloid Differentiation," *Exp. Hematol.*, 35:572-578 (2007) [Abstract only]. This abstract states that silencing of endogenous RTP801 by shRNA reduces retinoic acid-induced differentiation of the U937 cells and also abrogates hypoxia-induced inhibition of mTOR in those cells. This supports the statement of utility in the specification relating to treatment of a subject in need of treatment of hypoxia or ischemia-related disease.

Malagelada et al., "RTP801 is Elevated in Parkinson Brain Substantia Nigra Neurons and Mediates Death in Cellular Models of Parkinson's Disease by a Mechanism Involving Mammalian Target of Rapamycin Inactivation," *J. Neurosci.*, 26:9996-10005 (2006) [Abstract Only]. This abstract indicates that knockdown of RTP801 by short hairpin RNAs protects neurons against cell death in Parkinson's Disease models. This supports the disclosed statement of utility that antisense treatment will regulate apoptosis.

Corradetti et al., "The Stress-induced Proteins RTP801 and RTP801L are Negative Regulators of the Mammalian

Target of Rapamycin Pathway," *J. Biol. Chem.*, 280:9769-9772 (2005). This publication states that mTOR plays an essential role in cell growth control and that RTP801 potently inhibits signaling through mTOR. The article suggests that down-regulation of RTP801 would be useful to mediate stress-induced inhibition of the mTOR Pathway. Again, this supports the utility of treatment of those in need of treatment for hypoxia or ischemia-related disease.

Schwarzer et al., "REDD1 Integrates Hypoxia-mediated Survival Signaling Downstream of Phosphatidylinositol 3-kinase," *Oncogene*, 24:1138-1149 (2005) [Abstract Only]. This abstract indicates that RTP801 is also known as REDD1 and that reduced RTP801 levels can sensitize cells towards apoptosis. This supports the utility in the present specification relating to the regulation of apoptosis.

Brugarolas et al., "Regulation of mTOR Function in Response to Hypoxia by REDD1 and the TSC1/TSC2 Tumor Suppressor Complex," *Genes and Development*, 18:2893-2904 (2004). This publication indicates that the disruption of RTP801 abrogates the hypoxia-induced inhibition of mTOR. This also supports antagonism of RTP801 as a treatment for hypoxia or ischemia-related disease.

Brafman et al., "Inhibition of Oxygen-Induced Retinopathy in RTP801-Deficient Mice," *Invest. Ophomol. Vis.*

Sci., 45:3796-3805 (2004). This publication states that the expression of RTP801 was induced in the wild-type retina after hypoxia treatment, but in the absence of RTP801 expression, development of retinopathy in the mouse model of ROP was significantly attenuated, thus implying an important role of RTP801 in the pathogenesis of ROP. This is another further evidence for the utility of antagonizing RTP801 expression for the treatment of ischemia-related disease, such as retinopathy.

Shoshani et al., "Identification of a Novel Hypoxia-Inducible Factor 1-Responsive Gene, RTP801, Involved Apoptosis," *Mol. And Cell. Biol.*, 22:2283-2293 (2002). This reference supports the disclosed utility of regulation of apoptosis.

Richard et al., "Nonhypoxic Pathway Mediates the Induction of Hypoxia-Inducible Factor 1α in Vascular Smooth Muscle Cells," *J. Biol. Chem.*, 275:26765-26771 (2000). This reference also supports the disclosed utility of regulation of apoptosis.

Ellisen et al., "REDD1, A Developmentally Regulated Transcriptional Target of p63 and p53, Links p63 to Regulation of Reactive Oxygen Species," *Molecular Cell*, 10:995-1005 (2002). This reference also supports the disclosed utility of regulation of apoptosis.

Thus, there is ample evidence supporting the credibility of the statements of utility in the present specification. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 17, 20, 21 and 40 have also been rejected under 35 U.S.C. 112, first paragraph. The examiner states that since the claimed invention is not supported by either a well asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. This rejection is respectfully traversed.

It is established hereinabove that the present specification does state well asserted utilities. Thus, the 35 U.S.C. 112, first paragraph, how to use rejection should be withdrawn for the same reasons as discussed above with respect to the 35 U.S.C. 101 utility rejection. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 17, 20, 21 and 40 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The examiner states that this is a new matter rejection. The examiner states that the specification provides support for antisense that is entirely homologous to SEQ ID NO:2. The examiner states that reference to nucleic acids encoding SEQ ID NO:10 is broader than a

reference to SEQ ID NO:2 in view of the degeneracy of the genetic code. This rejection is respectfully traversed.

The present claims have now been amended so as not to rely on the sequence of the protein, but to instead rely on the sequence of the DNA. Claims 17 and 40 now refer to target mRNA corresponding to the cDNA of SEQ ID NO:2. As the examiner concedes that the specification provides support for antisense that is entirely homologous to SEQ ID NO:2, it is believed that this amendment now obviates the new matter rejection. Reconsideration and withdrawal thereof is therefore respectfully urged.

Claims 20 and 40 have been rejected under 35 U.S.C. 102(b), as being anticipated by Japanese patent 06303997 to Takagi. The examiner states that Takagi teaches amplification of mRNA using probes of 21 nucleotides that are complementary to nucleotides 1761-1781 of SEQ ID NO;2. This rejection is respectfully traversed.

The present claims are all directed to RNA molecules. The probes of Takagi are DNA probes. Accordingly, Takagi cannot anticipate the present application. Reconsideration and withdrawal of this rejection is therefore respectfully urged.

Claims 20 and 40 have been rejected under 35 U.S.C. 102(b), as being anticipated by Fodor that teaches an array

comprising all possible 10-mers. The examiner states that this rejection is asserted in view of the fact that the present claims only enjoy priority to the amendment filed on September 8, 2006. This rejection is respectfully traversed.

First, the claims have now been amended to obviate the new matter rejection and the examiner has indicated that claims specifying SEQ ID NO:2 rather than SEQ ID NO:10 would have an effective filing date in 1998, thus obviating this rejection.

Second, there is no authority in the patent statute, regulations or case law for assigning an effective filing date of a patent application for claims allegedly amended to contain new matter as of the date of the amendment inserting such alleged new matter. A claim cannot have an effective filing date later than the filing date of the application. Indeed, MPEP 2143.03 II states that limitations that do not find support in the original specification must still be considered when evaluating claims over the prior art. If a new matter rejection is overturned, then a post-filing date reference cannot be available as a reference. If the new matter rejection is not overturned, then the claims are unpatentable and it was a total waste of effort to cite references after the filing date of the application. The

examiner is invited to submit one source that would support such a position.

Finally, Fodor is supposed to teach an array of all possible 10-mers. However, as the publication does not write down all possible 10-mers, there can be no anticipation for the one that corresponds to an RNA within the scope of the present claims. This would only be an issue of obviousness. However, as Fodor does not teach the utility of the present application, the particular 10-mers that cover the mRNA of the present invention have unexpected properties and therefore would be unobviousness. For all of these reasons reconsideration and withdrawal of this rejection are respectfully urged.

It is submitted that all the claims now present in the case clearly defined over the references' of record and fully comply with 35 U.S.C. 112 and 35 U.S.C. 101. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By /rlb/
Roger L. Browdy
Registration No. 25,618

RLB:jmd
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
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